

CLAIMS

1. A solid pharmaceutical composition intended to be administered orally, characterized in that it comprises, within one and the same phase (internal phase):

- at least one solid and micronized lipophilic active principle,
- at least one surfactant,
- 10 - at least one cationic polymer insoluble in water at pH greater than or equal to 5, and
- at least one organic or inorganic acid.

2. The composition as claimed in claim 1, characterized in that the lipophilic active principle is chosen from blood lipid-reducing agents, steroid hormones, antifungal agents, retinoids, steroidal anti-inflammatories, nonsteroidal anti-inflammatories, anti-retroviral agents, protease inhibitors, antacids, 20 proton pump inhibitors, antiemetics, liposoluble vitamins, cardiovascular system drugs, anti-platelet aggregation agents, anticancer agents, certain plant extracts and their isolated or derived active principles, immunosuppressants, central nervous system drugs, antimigraine agents, antibiotics and anti-parasitic agents.

3. The composition as claimed in claim 2, characterized in that the blood lipid-reducing agents are chosen from 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoic acid 1-methylethyl ester (fenofibrate), bezafibrate, ciprofibrate, gemfibrozil, probucol, tiadenol, simvastatin, mevastatin, lovastatin, atorvastatin, pravastatin, fluvastatin, 35 cerivastatin and melinamide.

4. The composition as claimed in claim 2, characterized in that the steroid hormones are chosen from derived estrogens and esters of estradiol,

progesterone, danazol, testosterone and testosterone esters and derivatives, anti-androgens, 5 α -reductase inhibitors, competitive inhibitors of testosterone, quinazoline derivatives and nonsteroidal agonists/
5 antagonists of estrogen receptors.

5. The composition as claimed in claim 2, characterized in that the antifungal agents are chosen from itraconazole, miconazole, ketoconazole, fluconazole,
10 griseofulvin, amphotericin B and terbinafine.

6. The composition as claimed in any one of the preceding claims, characterized in that the lipophilic active principle is fenofibrate, progesterone or
15 itraconazole.

7. The composition as claimed in any one of the preceding claims, characterized in that the active principle represents from 10 to 90% by weight of the
20 total weight of the pharmaceutical composition.

8. The composition as claimed in any one of the preceding claims, characterized in that the surfactant is chosen from compounds having a hydrophilic-lipophilic balance (HLB) value greater than or equal to 15.
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9. The composition as claimed in claim 8, characterized in that the surfactant is chosen from sodium lauryl sulfate (HLB 40), poloxamers (HLB 16-29),
30 macrogol ethers of organic alcohols (HLB 15-18), and sucrose esters of organic acids (HLB 15-16).

10. The composition as claimed in claim 9, characterized in that the surfactant is sodium lauryl
35 sulfate.

11. The composition as claimed in any one of the preceding claims, characterized in that the surfactant

represents from 1 to 10% by weight of the total weight of said composition.

12. The composition as claimed in any one of the preceding claims, characterized in that the surfactant is in solid form.

13. The composition as claimed in claim 12, characterized in that the surfactant is comicronized with the active principle.

14. The composition as claimed in any one of the preceding claims, characterized in that the active principle/surfactant ratio by weight is between 100/1 and 5/1.

15. The composition as claimed in any one of the preceding claims, characterized in that the cationic polymers insoluble in water at pH greater than or equal to 5 are chosen from acrylic polymers comprising a tertiary amine group.

16. The composition as claimed in claim 15, characterized in that said polymers are chosen from polymers of aminoalkyl methacrylate type, soluble at pH below 5.

17. The composition as claimed in claim 16, characterized in that said polymers are chosen from the terpolymer of poly(dimethylaminoethyl methacrylate), of methyl methacrylate and of butyl methacrylate and the terpolymer of poly(diethylaminoethyl methacrylate), of methyl methacrylate and of butyl methacrylate.

18. The composition as claimed in any one of the preceding claims, characterized in that the cationic polymer(s) insoluble in water at pH greater than or equal to 5 represent(s) from 0.5 to 15% by weight

relative to the total weight of the pharmaceutical composition.

19. The composition as claimed in any one of the preceding claims, characterized in that the cationic polymer insoluble in water at pH greater than or equal to 5/active principle ratio by weight is between 1/5 and 1/30.

20. The composition as claimed in any one of the preceding claims, characterized in that the organic or inorganic acid is chosen from citric acid, succinic acid, fumaric acid, acetic acid, phosphoric acid, sulfuric acid and hydrochloric acid.

21. The composition as claimed in any one of the preceding claims, characterized in that the organic or inorganic acid represents from 1 to 10% by weight relative to the total weight of the composition.

22. The composition as claimed in any one of the preceding claims, characterized in that the organic or inorganic acid/cationic polymer insoluble in water at pH greater than or equal to 5 ratio by weight is between 6/1 and 0.25/1.

23. The composition as claimed in any one of the preceding claims, characterized in that the lipophilic active principle/inorganic or organic acid ratio is between 1/1 and 30/1.

24. The composition as claimed in any one of the preceding claims, characterized in that it comprises, by weight relative to the total weight of the composition:

- 40 to 80% of fenofibrate as lipophilic active principle,
- 2 to 10% of surfactant,
- 2 to 10% of a terpolymer of poly(dimethylamino-

ethyl methacrylate), of methyl methacrylate and
of butyl methacrylate, and
- from 2.5 to 5% of an inorganic or organic acid.

5 25. The composition as claimed in any one of the
preceding claims, characterized in that it comprises
fenofibrate as lipophilic active principle and in that
it is at least 50% dissolved in 15 minutes, more than
80% dissolved in 30 minutes, more than 85% dissolved in
10 45 minutes and more than 90% dissolved in 60 minutes,
as measured in accordance with the method using a
paddle rotating at 75 rpm according to the European
Pharmacopeia, in a dissolving medium consisting of 0.1M
sodium lauryl sulfate in aqueous solution brought to
15 37°C.

26. The composition as claimed in any one of the
preceding claims, characterized in that the internal
phase comprises one or more excipients chosen from
20 diluting agents and/or binders, disintegrating agents
and adjuvants for spraying, tableting, lubrication and
flow of powders.

27. The composition as claimed in any one of the
25 preceding claims, characterized in that it also
comprises an external phase comprising one or more
excipients.

28. A method for preparing a pharmaceutical
30 composition as defined in any one of claims 1 to 27,
characterized in that it comprises the following steps:

a) mixing of at least one solid and micronized
lipophilic active principle, of at least one
surfactant, of at least one cationic polymer insoluble
35 in water at pH greater than or equal to 5 and of at
least one organic or inorganic acid,

b) granulation or atomization of the mixture
obtained above in step a),

c) optional addition of an external phase comprising one or more excipients, then

d) tableting or dispensing into gelatin capsules of the mixture obtained at the end of step b) or c) when the latter is carried out.

29. The method as claimed in claim 28, characterized in that it comprises a preliminary step of comicronization of the active principle with the surfactant(s).

30. The method as claimed in claim 28 or 29, characterized in that step b) is carried out by granulation and in that the mixing of the constituents in step a) comprises the following substeps:

a1) preparing a solution or a suspension comprising at least one organic or inorganic acid and at least one cationic polymer insoluble in water at pH greater than or equal to 5, in a granulating liquid,

a2) spraying the mixture prepared above in step a1) onto the active principle which has been micronized and premixed with the solid surfactant or comicronized with said active principle, at a temperature compatible with the physical stability of the substances used in the formulation,

a3) recovering the fluidized granules thus obtained,

a4) calibrating the fluidized granules, and

a5) drying the fluidized granules.

31. The method as claimed in claim 30, characterized in that said polymer is a terpolymer of poly(dimethylaminoethyl methacrylate), of methyl methacrylate and of butyl methacrylate and in that the granulating liquid is a propanol/acetone mixture.

32. The method as claimed in claim 28 or 29, characterized in that step b) is carried out by

atomization and in that step a) comprises the following substeps:

5 a'1) preparing an acid or buffer solution comprising an inorganic or organic acid and a strong base, said solution having a pH of less than 5,

10 a'2) preparing a suspension by addition, to this buffer solution, of at least one solid and micronized lipophilic active principle, of at least one surfactant optionally comicronized with said active principle and of at least one cationic polymer insoluble in water at pH greater than or equal to 5, with stirring,

a'3) atomizing said suspension,

a'4) recovering the atomized product.